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Evaluation of Equine Albumin Solution in Fluid Therapy in Horses with Colic

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ABSTRACT

Equine albumin solution can be a good therapeutic option in fluid replacement for treatment of horses with colic. The purpose of this study was to evaluate the effects of initial fluid therapy with equine albumin solution in horses presenting with colic and mild-to-moderate dehydration, and to compare this therapy with fluid therapy based on crystalloids alone. Nineteen horses of both genders presenting with colic and mild-to-moderate dehydration were used. Animals were randomly assigned to one of two groups (control: fluid therapy based on crystalloid solutions; experimental: fluid therapy based on equine albumin and crystalloid solutions). Physical examination, hematocrit determination, blood gas analysis, serum biochemistry, blood and peritoneal lactate assessment, and measurement of colloid osmotic and arterial pressure were performed at predetermined times. Good results were obtained with equine albumin solution. More fluid is attracted into and maintained in the intravascular compartment, despite infusion of small volumes, as indicated by higher arterial pressure, lower capillary refill time, lower hematocrit and serum protein concentrations, lower colloid osmotic pressure, and better skin turgor. Equine albumin solution has good oncotic action and is a safe fluid therapy option for horses with colic and mild-to-moderate dehydration. Our results suggest it can be a good choice of fluid for correction of severe dehydration, although further research is necessary to determine the adequate dose in such cases.

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1. Introduction

Albumin is present in 5% or 25% solutions at 96% purity and can be used as a colloidal agent in humans [1].

In horses, crystalloids are used more often than colloids even in cases of severe hypovolemia because of their lower price and lower risk of side effects [2]. However, fluid replacement with crystalloids alone may not be enough to re-establish adequate circulation in cases of acute

circulatory failure or severe dehydration (often seen in horses with colic), where hypertonic saline or colloid solutions may be indicated more [3,4].

To date, species-specific plasma is the most commonly used colloid in horses, despite its decreased ability to increase oncotic pressure owing to rapid redistribution of proteins into the extravascular space [5]. Synthetic colloids have only transient effects on plasma volume and are devoid of other functions, such as the transport of substances [1].

The use of albumin as a colloid in horses could have many advantages. The primary action of albumin is maintenance of oncotic pressure, but it also helps transport many substances, ligates reversibly with cations and anions, and is a free radical scavenger [6].

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Few references to the use of albumin in animals were found in the literature and most involve the use of human albumin. Several experimental studies were performed with good results in laboratory animals [7], dogs [8], sheep [9], and guinea pigs [10].

Reports and studies on clinical cases refer to the use of human albumin in small animals and horses, given that albumin obtained from other species is not commercially available [6,11]. Trow et al. [12] reported good results, with increase in serum albumin concentration and oncotic pressure, after the use of 10% albumin in 73 dogs suffering from different conditions. Viganó et al. [13] reported good safety after the use of 5% human albumin in small animals presenting with hypoalbuminemia. Both studies reported frequent occurrence of low-grade side effects.

There is only one previous study that evaluated the behavior of homologous albumin in horses [14]. In that experiment, fluid therapy with concentrated equine albumin (5% in normal saline) was compared with fluid therapy with normal saline solution alone for treatment of induced mild-to-moderate dehydration. The authors concluded that the albumin solution is easy to prepare and to infuse and has no adverse effects and that a small volume of the solution has similar effects to infusion under pressure of half the calculated volume of saline solution for hydration of the same animal.

Equine albumin solution may be a good option for treatment of horses with colic, particularly in shock situations; in cases where hypoproteinemia is a concern; and for raising arterial pressure in patients who require surgical intervention. However, the correct dose and speed of administration must be established in healthy animals before the fluid can be used in clinical situations.

The purpose of this study was to evaluate the effects of equine albumin solution in initial fluid therapy in horses presenting with colic and mild-to-moderate dehydration and to compare it with fluid therapy based on crystalloids alone.

2. Materials and Methods

2.1. Animals

Nineteen horses of both genders presenting with colic due to different causes and with mild-to-moderate dehydration to the Veterinary Hospital of the Faculdade de Medicina Veterinária e Zootecnia da Universidade de São Paulo were selected.

Animals were randomly assigned to one of two groups (CG [control]: fluid therapy based on crystalloid solutions; EG [experimental]: fluid therapy based on equine albumin and crystalloid solutions).

2.2. Initial Assessment

Initial assessment of all animals was performed according to the standard protocol adopted at the Veterinary Hospital and included signalment; weighing; anamnesis; general physical assessment; abdominal, cardiac, and pulmonary auscultation; nasogastric tubing; abdominocentesis; rectal palpation; and hematocrit determination.

Arterial blood was sampled for blood gas analysis; total blood without anticoagulant was sampled for determination of total serum protein, albumin, urea, creatinine, aspartate aminotransferase (AST), γ -glutamyl transferase (GGT), and bilirubin; and total blood with anticoagulant was sampled for complete blood cell count. Colloid osmotic pressure and blood and peritoneal lactate were assessed. Arterial pressure was measured at the coccygeal artery using a sphygmomanometer and Doppler ultrasonography.

Biochemical workup was performed to assess the initial state of the patient (severity of the colic) and the changes during and/or after fluid therapy in both groups (CG and EG).

The hematocrit was determined using a microcapillary tube and a centrifuge. Blood gas variables were quantified using an automatic pH and blood gas analyser (OMNI Modular System, AVL, Roche Diagnostics, Graz, Austria). Serum total protein, albumin, AST, GGT, bilirubin, urea, and creatinine were quantified using an automatic biochemical analyser (Lyasis, AMS Diagnostics, Summerville, South Carolina, EUA). Lactate was measured with a portable lactometer (Accutrend, Roche, Mannheim, Germany). Colloid osmotic pressure was quantified using a colloid osmometer (model 4420, Wescor, Utah, USA).

2.3. Fluid Therapy Calculation and Administration

The level of dehydration was estimated based on skin turgor, hematocrit, and capillary refill time (CRT), according to the table given by Seahorn and Cornick-Seahorn [15]. The volume of fluid to be replaced was calculated as body weight multiplied by the estimated percentage of dehydration.

After estimation of the percentage of dehydration and calculation of the volume of fluid to be replaced, intravenous fluid therapy was started, based on the group involved (CG or EG), as follows: continuous infusion of crystalloid solution alone (CG), and continuous infusion of albumin solution followed by crystalloid solution (EG).

The crystalloid of choice was lactated Ringer's solution. The albumin used in the EG was manufactured [16] and provided by Instituto Butantan (Brazilian government-owned research center) in lyophilized form in 35-mL vials. This product was used for preparation of the 5% solution (in normal saline) administered to the patients. The final dose per animal was 8 mL/kg body weight, based on the mean volume used in a previous experiment with the same solution [14].

2.4. Assessment During Fluid Therapy

During fluid therapy, heart and respiratory rates, mucous membrane color, CRT, skin turgor, arterial pressure, blood gas analysis, hematocrit, serum total protein, and albumin concentrations were reassessed.

Reassessments were performed after administration of the albumin solution (EG) and at 30, 60, and 120 minutes after crystalloid solution administration was started (EG and CG). Whenever the calculated volume of fluid could not be given within this interval, an additional reassessment was performed at the end of the fluid therapy. Reassessment times (T) were sequentially numbered throughout

Table 1

Correspondence between experimental times in each group

Experimental Times	Control Group (CG)	Experimental Group (EG)
T0	Before fluid therapy	Before fluid therapy
T1	30 minutes after administration of crystalloids was started	After administration of albumin solution
T2	60 minutes after administration of crystalloids was started	30 minutes after administration of crystalloids was started
T3	120 minutes after administration of crystalloids was started or end of fluid therapy	60 minutes after administration of crystalloids was started
T4	End of fluid therapy	120 minutes after administration of crystalloids was started or end of fluid therapy
T5	–	End of fluid therapy

the experiment (Table 1). Urea, creatinine, and blood and peritoneal lactate were also reassessed after fluid therapy.

Data were statistically compared before and after fluid therapy and between the two groups. Statistical analysis was performed using GraphPad InStat (version 3.01, 1998, GraphPad Software, San Diego, CA, USA).

This project was approved by the Bioethics Committee of the Faculdade de Medicina Veterinária e Zootecnia da Universidade de São Paulo (protocol 933/2006).

3. Results and Discussion

Horses of different pure breeds (Mangalarga, Standardbred, Appaloosa, Brazilian Sport Horse, and Quarter Horse) and of mixed breeds were included in the study. There were 14 male (seven in each group) and five female (three in the CG and two in the EG) horses. The causes of colic included three cases of nephrosplenic entrapment, three cases of large-colon impaction, two cases of enteroliths, two cases of large-colon displacement, and one case each of epiploic foramen entrapment, inguinal ring entrapment, small-colon impaction, foreign body in the small colon, cecocolic intussusception, cecal distention, anterior enteritis, gastric overload with gastritis, and postovulation hemoperitoneum.

Mean age of the patients was 11.60 ± 7.05 years (ranging from 3 to 22 years) in the CG and 9.33 ± 6.20 (ranging from 2 to 19 years) in the EG, with no statistical difference between groups ($P = .4696$). Mean body weight was 445.0 ± 70.2 kg in the CG and 424.1 ± 61.9 kg in the EG, with no statistical difference between groups ($P = .5035$).

Complete blood cell count, AST, GGT, bilirubin, and fibrinogen determinations were performed only at the beginning of the clinical evaluation as part of a standard protocol for colic cases and to rule out other concurrent conditions that might interfere with the results of this study. Two animals (animal 2 in the CG and animal 8 in the EG) had prerenal azotemia that was not totally reversed after the proposed fluid therapy but resolved without further complications as treatment progressed.

Mean dehydration was $4.9\% \pm 0.9\%$ in the CG and $5.1\% \pm 1.1\%$ in the EG, with no statistical difference between groups ($P = .6756$).

Some data could not be obtained from all patients at all times, as the need for urgent surgical intervention precluded complete hydration in some cases. In other cases, animals were too restless to allow collection of all samples and data. However, this did not compromise the experiment, given that the most important results lie within times

0 and 1 hour, when all variables could be obtained. Also, the idea behind this project was to work with clinical cases to evaluate the feasibility of the proposed procedures and treatments, and thus our final results are directly applicable to clinical situations.

There are no reports of adverse side effects of plasma transfusion in horses in the literature [17], although other authors have observed such reactions in foals only [18].

In humans, some complications are reported with albumin solution, including transfusion-like reactions, hypocalcemia, decreased initial urine output, and pulmonary edema [19]. Allergic reactions are rare, and the risk of pulmonary dysfunction seems to be more related with the original condition than with the type of fluid used [1]. Moreover, despite ongoing controversy, there are studies showing that albumin is safer than synthetic colloids in humans [20]. Side effects related to the use of human albumin have been reported in small animals; however, these side effects tended to be of less significance [12,13].

As in previous studies [14], our results suggest that the use of albumin solution is safe, given that no side effects were observed. This may be because of the level of purity of the product used and the fact that it was species specific. When human albumin is used in other species, the risk of immediate or late adverse reaction is higher [6].

The lyophilized preparation was evaluated. This preparation is more practical for storage and is not prone to contamination, as is the case with the fresh refrigerated bags used in a previous study [14], although the small volume contained in each vial increases the time required for preparation of the final solution. Given the goal is to use the product in patients suffering from severe dehydration or shock, which might require larger volumes than those used here, the time required for preparation of the solution is a possible downside of this preparation.

During fluid therapy, heart and respiratory rates, body temperature, and cecal movements varied more according to the original condition than to the hydration. Body temperature tended to drop during fluid therapy, possibly

Table 2

Mean and standard deviation of systolic arterial pressure (mm Hg) of animals in the control (CG) and experimental (EG) groups at different times

Group	T0	T1	T2	T3	P
CG	13.70 ± 2.57	14.35 ± 2.35	14.55 ± 2.24	13.43 ± 1.05	.7546
EG	12.38 ± 3.18	13.05 ± 2.43	13.94 ± 1.92	14.06 ± 2.06	.4490
P	.3348	.2551	.5385	.4573	

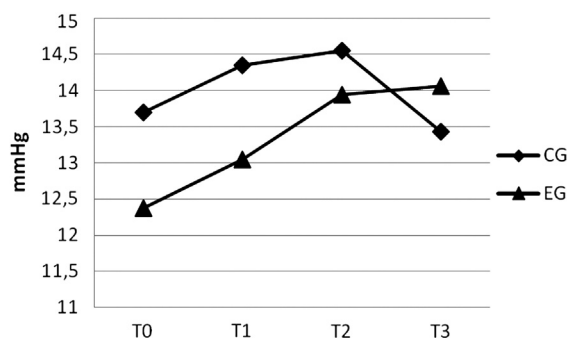


Fig. 1. Systolic arterial pressure (mm Hg) of animals in the control (CG) and experimental (EG) groups at different times.

because the fluid was not warmed before administration. This was statistically significant in the EG between T0 (37.77 ± 0.37) and T1 (37.24 ± 0.56) ($P = .0207$) but did not differ between groups. The statistical difference observed in the EG may reflect the influence of room temperature or the small number of subjects studied. There is no reason why albumin should cause a decrease in body temperature in animals, and in humans, the expected reaction would be one of hyperthermia.

Mucous membrane color tended to improve with fluid therapy in both groups, with no statistical difference between groups. The variations of this variable were mostly related to the original condition.

Blood gas variables were generally within normal limits in both groups at all times. The few changes observed, mostly in bicarbonate and base excess values, seemed to be more related to the original condition than to fluid therapy. Respiratory changes, listed in the literature as one of the possible complications related to the use of albumin in humans, were not observed in this or in a previous study [14]. Respiratory rates actually decreased more in the EG, with significant ($P = .0378$) differences between T1 (17.7 ± 6.3) and T2 (29.3 ± 13.2) and with no significant differences between groups. Should albumin cause respiratory changes related to pulmonary edema, an increase in respiratory rates would be expected and not otherwise.

Serum urea and creatinine values did not differ significantly before and after fluid therapy or between groups, although values tended to drop in most patients, possibly reflecting the correction of prerenal azotemia, as expected after fluid therapy.

Blood and peritoneal lactate values did not vary significantly between times or groups. This variable, particularly peritoneal lactate, has a good correlation with the prognosis in cases of colic [21] but is not strongly correlated with the responses to initial treatment.

Arterial pressure (systolic, diastolic, and mean values) tended to increase during fluid therapy, particularly in patients presenting with lower arterial pressure. In the remaining patients, arterial pressure remained stable or decreased slightly when values were initially high due to pain. Systolic arterial pressure values (mean and standard deviation) are given in Table 2 and Figure 1.

A similar pattern of nonsignificant increase in arterial pressure due to great individual variation was reported in other studies [14,22]. It should be noted that the increase in arterial pressure in the EG (T1) was due to the oncotic action of albumin solution, given that the volume infused was not large enough to cause such an increase. A long-lasting hemodynamic improvement of up to 36 hours after albumin infusion is also observed in humans [23].

CRTs decreased with fluid therapy in both groups. Differences between T1 (2.20 ± 0.42 seconds) and T0 (2.40 ± 0.51 seconds) were nonsignificant in the CG ($P = .3434$) and significant in the EG ($T0 = 2.55 \pm 0.52$; $T1 = 2.00 \pm 0.50$; $P = .0133$). In T1, the fact that horses in the EG received albumin solution only (3.0–4.5 L, depending on body weight) and those in the CG received a larger amount of fluid (almost twice as much in some cases) suggests that the colloidal action of albumin led to greater fluid retention in the intravascular compartment.

The same rationale can be extrapolated to interpret skin turgor responses. Values decreased significantly ($P = .0150$) between T0 (2.50 ± 0.70) and T1 (2.00 ± 0.94) in the CG, with no significant differences in the EG ($T0 = 2.44 \pm 0.88$; $T1 = 2.33 \pm 0.70$; $P = .3466$), suggesting a rapid fluid shift from the intravascular to the interstitial space. After fluid therapy, the hematocrit decreased significantly in both groups (Table 3), as expected. Differences were significant between T0 and T1 and between T0 and time of last data collection but not between groups, again suggesting a useful osmotic action of the equine albumin solution.

Serum total protein followed a similar pattern, decreasing significantly with fluid therapy between T0 and T1 in both groups (CG: $P = .0001$; EG: $P = .0003$), with no significant differences between groups. Albumin also decreased significantly with fluid therapy between T0 and T1 in both groups (CG: $P = .0337$; EG: $P = .0018$), with no significant differences between groups. Although the EG was given exogenous albumin, the colloidal action was greater than the increase observed in albumin serum dosage. A large increase in serum albumin concentration was not expected because the volume infused was small and because a greater intravascular fluid retention to the detriment of serum albumin concentration has been described [14] in horses with induced mild-to-moderate dehydration, even though serum albumin concentrations tended to be higher in the EG than in the CG in this study.

Table 3

Mean and standard deviation of the hematocrit (%) of animals in the control (CG) and experimental (EG) groups at different times

Group	T0	T1	T2	T3	P
CG	42.30 ± 5.77^a	35.10 ± 5.68^b	34.70 ± 4.71^{bc}	32.50 ± 4.84^d	.0019*
EG	39.11 ± 6.47^a	33.55 ± 5.12^b	32.25 ± 5.33^b	32.37 ± 5.04^b	.0465*
P	.2719	.5441	.4434	.9604	

Different letters in the same row indicate significant difference.

* Significant difference.

Table 4

Mean values and standard deviation of colloid osmotic pressure (mm Hg) of animals in the control (CG) and experimental (EG) groups

Group	T0	T1	T2	T3	T4	P
CG	26.98 ± 5.2 ^a	23.15 ± 3.5 ^b	22.1 ± 3.4 ^c	21.36 ± 3.2 ^d	21.5 ± 3.9	.0217*
EG	26.03 ± 3.7 ^a	22.41 ± 3.7 ^b	20.76 ± 4.14 ^c	18.78 ± 2.7 ^c	17.92 ± 2.5	.0022*
P	.6584	.6642	.4674	.1130	.1781	

T4 was not included in the statistical analysis owing to the low number of samples obtained.

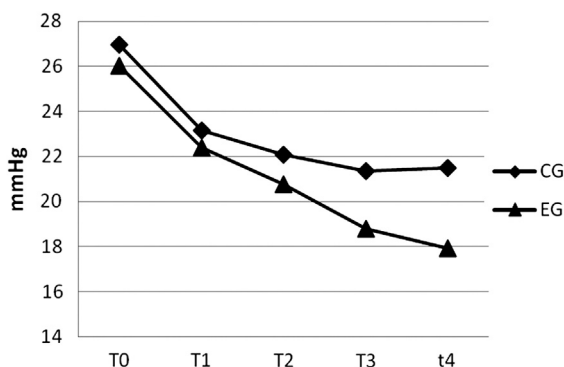
Different letters in the same row indicate statistically significant difference.

* Significant difference.

Results concerning plasma colloid osmotic pressure readings obtained by means of a colloid osmometer are displayed in Table 4. T4 was not included in the statistical analysis because of the small number of samples obtained. Direct readings of colloid osmotic pressure are much more precise than its estimation using mathematical equations. Fluid therapy led to a decrease in colloid osmotic pressure in both groups. This was expected, given that the fluid used in large volumes was a crystalloid (lactated Ringer's solution), which has a lower oncotic pressure than blood. Colloid osmotic pressure in T0 and T1 did not differ significantly between groups but differed significantly within each group. The lack of difference in T1 between groups reflects the colloidal action of albumin, given that the small volume of crystalloid used in the preparation of the albumin solution could not have accounted for such changes in colloid osmotic pressure.

Human albumin led to an increase in serum albumin concentration and oncotic pressure in dogs [12]. This was not observed in this study. However, in the study in dogs, larger amounts were infused and oncotic pressure was not assessed right after infusion, as in this study, where the purpose was to demonstrate the effects of plasma expansion and where animals did not have hypoalbuminemia.

Colloid osmotic assessment was a good method to demonstrate the shift of fluid to the intravascular space. Despite the lack of significant differences between groups at the end of the fluid therapy, values tended to be lower in the EG (Fig. 2). It should be noted that fluid therapy was generally more prolonged in the EG than in the CG owing to the inclusion of an additional step (albumin delivery) in the procedure in that group. A greater fluid redistribution and smaller fluid retention could thus be expected but was not observed.

**Fig. 2.** Colloid osmotic pressure (mm Hg) of animals in the control (CG) and experimental (EG) groups at different times.

Equine albumin had a good oncotic action, increasing the fluid shift to the intravascular space, despite the small volumes infused, as suggested by the increase in arterial pressure, lower CRT, lower hematocrit and serum total protein, reduced colloid osmotic pressure, and maintenance of skin turgor.

Despite the good results obtained with equine albumin solution in horses in this study, further research is needed to determine the dose required for treatment of emergencies involving severe dehydration/shock, and this cannot be extrapolated from this study.

4. Conclusions

Equine albumin solution is a safe colloid for use in horses suffering from colic with mild-to-moderate dehydration. It might be a good choice of colloid for treatment of severe dehydration, but further studies are necessary to determine the best dose in such cases.

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